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NOTICE OF ALLOWANCE AND FEE(S) DUE

28061 7590 10/03/2008

THEODORE J. BIELEN JR.
BIELEN, LAMPE, & THOEMING
1390 WILLOW PASS ROAD
SUITE 1020
CONCORD, CA 94520

| | |
|-------------------|--------------|
| EXAMINER | |
| PARKIN, JEFFREY S | |
| ART UNIT | PAPER NUMBER |
| 1648 | |

DATE MAILED: 10/03/2008

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|-----------------|-------------|----------------------|---------------------|------------------|
| 10/811,725 | 03/29/2004 | Sateesh Apte | 14705 | 1415 |

TITLE OF INVENTION: NEF DELETED HUMAN IMMUNODEFICIENCY VIRUS FOR THE RESTORATION OF T-LYMPHOCYTE SIGNALLING AND ACTIVATION FOR THE TREATMENT AND PREVENTION OF HUMAN IMMUNODEFICIENCY VIRUS INFECTION

| APPLN. TYPE | SMALL ENTITY | ISSUE FEE DUE | PUBLICATION FEE DUE | PREV. PAID ISSUE FEE | TOTAL FEE(S) DUE | DATE DUE |
|----------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | YES | \$755 | \$0 | \$0 | \$755 | 01/05/2009 |

THE APPLICATION IDENTIFIED ABOVE HAS BEEN EXAMINED AND IS ALLOWED FOR ISSUANCE AS A PATENT. PROSECUTION ON THE MERITS IS CLOSED. THIS NOTICE OF ALLOWANCE IS NOT A GRANT OF PATENT RIGHTS. THIS APPLICATION IS SUBJECT TO WITHDRAWAL FROM ISSUE AT THE INITIATIVE OF THE OFFICE OR UPON PETITION BY THE APPLICANT. SEE 37 CFR 1.313 AND MPEP 1308.

THE ISSUE FEE AND PUBLICATION FEE (IF REQUIRED) MUST BE PAID WITHIN THREE MONTHS FROM THE MAILING DATE OF THIS NOTICE OR THIS APPLICATION SHALL BE REGARDED AS ABANDONED. THIS STATUTORY PERIOD CANNOT BE EXTENDED. SEE 35 U.S.C. 151. THE ISSUE FEE DUE INDICATED ABOVE DOES NOT REFLECT A CREDIT FOR ANY PREVIOUSLY PAID ISSUE FEE IN THIS APPLICATION. IF AN ISSUE FEE HAS PREVIOUSLY BEEN PAID IN THIS APPLICATION (AS SHOWN ABOVE), THE RETURN OF PART B OF THIS FORM WILL BE CONSIDERED A REQUEST TO REAPPLY THE PREVIOUSLY PAID ISSUE FEE TOWARD THE ISSUE FEE NOW DUE.

HOW TO REPLY TO THIS NOTICE:

I. Review the SMALL ENTITY status shown above.

If the SMALL ENTITY is shown as YES, verify your current SMALL ENTITY status:

A. If the status is the same, pay the TOTAL FEE(S) DUE shown above.

B. If the status above is to be removed, check box 5b on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and twice the amount of the ISSUE FEE shown above, or

If the SMALL ENTITY is shown as NO:

A. Pay TOTAL FEE(S) DUE shown above, or

B. If applicant claimed SMALL ENTITY status before, or is now claiming SMALL ENTITY status, check box 5a on Part B - Fee(s) Transmittal and pay the PUBLICATION FEE (if required) and 1/2 the ISSUE FEE shown above.

II. PART B - FEE(S) TRANSMITTAL, or its equivalent, must be completed and returned to the United States Patent and Trademark Office (USPTO) with your ISSUE FEE and PUBLICATION FEE (if required). If you are charging the fee(s) to your deposit account, section "4b" of Part B - Fee(s) Transmittal should be completed and an extra copy of the form should be submitted. If an equivalent of Part B is filed, a request to reapply a previously paid issue fee must be clearly made, and delays in processing may occur due to the difficulty in recognizing the paper as an equivalent of Part B.

III. All communications regarding this application must give the application number. Please direct all communications prior to issuance to Mail Stop ISSUE FEE unless advised to the contrary.

IMPORTANT REMINDER: Utility patents issuing on applications filed on or after Dec. 12, 1980 may require payment of maintenance fees. It is patentee's responsibility to ensure timely payment of maintenance fees when due.

PART B - FEE(S) TRANSMITTAL

Complete and send this form, together with applicable fee(s), to: **Mail Stop ISSUE FEE**
Commissioner for Patents
P.O. Box 1450
Alexandria, Virginia 22313-1450
or Fax (571)-273-2885

INSTRUCTIONS: This form should be used for transmitting the ISSUE FEE and PUBLICATION FEE (if required). Blocks 1 through 5 should be completed where appropriate. All further correspondence including the Patent, advance orders and notification of maintenance fees will be mailed to the current correspondence address as indicated unless corrected below or directed otherwise in Block 1, by (a) specifying a new correspondence address; and/or (b) indicating a separate "FEE ADDRESS" for maintenance fee notifications.

CURRENT CORRESPONDENCE ADDRESS (Note: Use Block 1 for any change of address)

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Note: A certificate of mailing can only be used for domestic mailings of the Fee(s) Transmittal. This certificate cannot be used for any other accompanying papers. Each additional paper, such as an assignment or formal drawing, must have its own certificate of mailing or transmission.

Certificate of Mailing or Transmission

I hereby certify that this Fee(s) Transmittal is being deposited with the United States Postal Service with sufficient postage for first class mail in an envelope addressed to the Mail Stop ISSUE FEE address above, or being facsimile transmitted to the USPTO (571) 273-2885, on the date indicated below.

| |
|--------------------|
| (Depositor's name) |
| (Signature) |
| (Date) |

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|-------------------|--------------|---------------|---------------------|----------------------|------------------|------------|
| nonprovisional | YES | \$755 | \$0 | \$0 | \$755 | 01/05/2009 |
| EXAMINER | | ART UNIT | CLASS-SUBCLASS | | | |
| PARKIN, JEFFREY S | | 1648 | 424-188100 | | | |

1. Change of correspondence address or indication of "Fee Address" (37 CFR 1.363).

Change of correspondence address (or Change of Correspondence Address form PTO/SB/122) attached.
 "Fee Address" indication (or "Fee Address" Indication form PTO/SB/47; Rev 03-02 or more recent) attached. **Use of a Customer Number is required.**

2. For printing on the patent front page, list
 (1) the names of up to 3 registered patent attorneys or agents OR, alternatively,
 (2) the name of a single firm (having as a member a registered attorney or agent) and the names of up to 2 registered patent attorneys or agents. If no name is listed, no name will be printed.

1 _____
 2 _____
 3 _____

3. ASSIGNEE NAME AND RESIDENCE DATA TO BE PRINTED ON THE PATENT (print or type)

PLEASE NOTE: Unless an assignee is identified below, no assignee data will appear on the patent. If an assignee is identified below, the document has been filed for recordation as set forth in 37 CFR 3.11. Completion of this form is NOT a substitute for filing an assignment.

(A) NAME OF ASSIGNEE

(B) RESIDENCE: (CITY and STATE OR COUNTRY)

Please check the appropriate assignee category or categories (will not be printed on the patent): Individual Corporation or other private group entity Government

4a. The following fee(s) are submitted:

Issue Fee
 Publication Fee (No small entity discount permitted)
 Advance Order - # of Copies _____

4b. Payment of Fee(s): (Please first reapply any previously paid issue fee shown above)

A check is enclosed.
 Payment by credit card. Form PTO-2038 is attached.
 The Director is hereby authorized to charge the required fee(s), any deficiency, or credit any overpayment, to Deposit Account Number _____ (enclose an extra copy of this form).

5. Change in Entity Status (from status indicated above)

a. Applicant claims SMALL ENTITY status. See 37 CFR 1.27. b. Applicant is no longer claiming SMALL ENTITY status. See 37 CFR 1.27(g)(2).

NOTE: The Issue Fee and Publication Fee (if required) will not be accepted from anyone other than the applicant; a registered attorney or agent; or the assignee or other party in interest as shown by the records of the United States Patent and Trademark Office.

Authorized Signature _____

Date _____

Typed or printed name _____

Registration No. _____

This collection of information is required by 37 CFR 1.311. The information is required to obtain or retain a benefit by the public which is to file (and by the USPTO to process) an application. Confidentiality is governed by 35 U.S.C. 122 and 37 CFR 1.14. This collection is estimated to take 12 minutes to complete, including gathering, preparing, and submitting the completed application form to the USPTO. Time will vary depending upon the individual case. Any comments on the amount of time you require to complete this form and/or suggestions for reducing this burden, should be sent to the Chief Information Officer, U.S. Patent and Trademark Office, U.S. Department of Commerce, P.O. Box 1450, Alexandria, Virginia 22313-1450. DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

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| 1390 WILLOW PASS ROAD | | | | PAPER NUMBER |
| SUITE 1020 | | | | 1648 |
| CONCORD, CA 94520 | | | | DATE MAILED: 10/03/2008 |

Determination of Patent Term Adjustment under 35 U.S.C. 154 (b)

(application filed on or after May 29, 2000)

The Patent Term Adjustment to date is 700 day(s). If the issue fee is paid on the date that is three months after the mailing date of this notice and the patent issues on the Tuesday before the date that is 28 weeks (six and a half months) after the mailing date of this notice, the Patent Term Adjustment will be 700 day(s).

If a Continued Prosecution Application (CPA) was filed in the above-identified application, the filing date that determines Patent Term Adjustment is the filing date of the most recent CPA.

Applicant will be able to obtain more detailed information by accessing the Patent Application Information Retrieval (PAIR) WEB site (<http://pair.uspto.gov>).

Any questions regarding the Patent Term Extension or Adjustment determination should be directed to the Office of Patent Legal Administration at (571)-272-7702. Questions relating to issue and publication fee payments should be directed to the Customer Service Center of the Office of Patent Publication at 1-(888)-786-0101 or (571)-272-4200.

| | | | |
|-------------------------------|--------------------------|---------------------|--|
| Notice of Allowability | Application No. | Applicant(s) | |
| | 10/811,725 | APTE, SATEESH | |
| | Examiner | Art Unit | |
| | Jeffrey S. Parkin, Ph.D. | 1648 | |

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address--**

All claims being allowable, PROSECUTION ON THE MERITS IS (OR REMAINS) CLOSED in this application. If not included herewith (or previously mailed), a Notice of Allowance (PTO-85) or other appropriate communication will be mailed in due course. **THIS NOTICE OF ALLOWABILITY IS NOT A GRANT OF PATENT RIGHTS.** This application is subject to withdrawal from issue at the initiative of the Office or upon petition by the applicant. See 37 CFR 1.313 and MPEP 1308.

1. This communication is responsive to the communications filed 01/07/08, 02/11/08, and 08/15/08.
2. The allowed claim(s) is/are 1 and 2.
3. Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
 - a) All
 - b) Some*
 - c) None
 of the:
 1. Certified copies of the priority documents have been received.
 2. Certified copies of the priority documents have been received in Application No. _____.
 3. Copies of the certified copies of the priority documents have been received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

* Certified copies not received: _____.

Applicant has THREE MONTHS FROM THE "MAILING DATE" of this communication to file a reply complying with the requirements noted below. Failure to timely comply will result in ABANDONMENT of this application.

THIS THREE-MONTH PERIOD IS NOT EXTENDABLE.

4. A SUBSTITUTE OATH OR DECLARATION must be submitted. Note the attached EXAMINER'S AMENDMENT or NOTICE OF INFORMAL PATENT APPLICATION (PTO-152) which gives reason(s) why the oath or declaration is deficient.
5. CORRECTED DRAWINGS (as "replacement sheets") must be submitted.
 - (a) including changes required by the Notice of Draftsperson's Patent Drawing Review (PTO-948) attached
 - 1) hereto or 2) to Paper No./Mail Date _____.
 - (b) including changes required by the attached Examiner's Amendment / Comment or in the Office action of Paper No./Mail Date _____.

Identifying indicia such as the application number (see 37 CFR 1.84(c)) should be written on the drawings in the front (not the back) of each sheet. Replacement sheet(s) should be labeled as such in the header according to 37 CFR 1.121(d).
6. DEPOSIT OF and/or INFORMATION about the deposit of BIOLOGICAL MATERIAL must be submitted. Note the attached Examiner's comment regarding REQUIREMENT FOR THE DEPOSIT OF BIOLOGICAL MATERIAL.

Attachment(s)

1. Notice of References Cited (PTO-892)
2. Notice of Draftsperson's Patent Drawing Review (PTO-948)
3. Information Disclosure Statements (PTO/SB/08),
Paper No./Mail Date _____
4. Examiner's Comment Regarding Requirement for Deposit
of Biological Material
5. Notice of Informal Patent Application
6. Interview Summary (PTO-413),
Paper No./Mail Date _____.
7. Examiner's Amendment/Comment
8. Examiner's Statement of Reasons for Allowance
9. Other _____.

Detailed Office Action

Status of the Claims

Acknowledgement is hereby made of receipt and entry of the communications filed 07 January, 2008, 11 February, 2008, and 15 August, 2008. The amendment-after-final submitted 07 January, 2008, will entered. After entry of this amendment, claims 1, 2, and 4-8 will pending in the instant application. The amendment-after-final submitted 11 February, 2008, will also be entered. After entry of this amendment claims 1, 2, and 4-6 will be pending in the instant application. Claims 4-6 stand withdrawn from further consideration by the examiner, pursuant to 37 C.F.R. § 1.142(b), as being drawn to a nonelected invention. The election was made without traverse.

Examiner's Amendment

An Examiner's Amendment to the record appears below. Should the changes and/or additions be unacceptable to applicant, an amendment may be filed as provided by 37 C.F.R. § 1.312. To ensure consideration of such an amendment, it **MUST** be submitted no later than the payment of the Issue Fee.

1. The application has been amended as follows:

- Please amend the TITLE as follows: **Pharmaceutical compositions comprising attenuated HIV-1 nef-deficient viral particles.**

- Please amend the first paragraph of the specification to read as follows: This application is a Continuation-in-Part of Application No.: 08/879,099, filed 19 June, 1997, **now U.S. Patent No. 6,713,064.**

- Please cancel claims 4-6 without prejudice or disclaimer. These claims were directed to an invention elected without traverse. Refer to M.P.E.P. § 821.02. Applicant is reminded that where a reply to a final action has otherwise placed the application in condition for allowance, the failure to cancel claims drawn to the nonelected invention or to take appropriate action will be construed as authorization to cancel these claims by examiner's amendment and pass the application to issue after the expiration of the period for reply.

35 U.S.C. § 120 Benefit

Applicant is advised that U.S. Serial No. 08/879,099, filed 19 June, 1997, is a Continuation of Application No.: 08/364,600, filed 27 December, 1994, now abandoned. If applicant desires to claim the benefit of a prior-filed application under 35 U.S.C. § 120, a specific reference to the prior-filed application in compliance with 37 C.F.R. § 1.78(a) **must** be included in the first sentence(s) of the specification following the title **or** in an application data sheet. For benefit claims under 35 U.S.C. § 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. **If the instant application is a utility or plant application filed under 35 U.S.C. § 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application.** If the application is a utility or plant application which entered the

national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. § 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. § 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 C.F.R. § 1.78(a)(2)(ii) and (a)(5)(ii). **This time period is not extendable and a failure to submit the reference required by 35 U.S.C. § 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. § 119(e), 120, 121 and 365(c).** A benefit claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed benefit claim under 35 U.S.C. § 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. § 120 or 119(e) and 37 C.F.R. § 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 C.F.R. § 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 C.F.R. § 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450. If the reference to the prior application was previously submitted within the time period set forth in 37 C.F.R. § 1.78(a), but not in the first sentence(s) of the specification or an application data sheet (ADS) as required by 37 C.F.R. § 1.78(a) (e.g., if the reference was submitted in an oath or declaration or the application transmittal letter), and the information concerning the benefit claim was recognized by the Office as shown by its inclusion on the first filing receipt, the petition under 37 C.F.R. § 1.78(a) and the surcharge under 37 C.F.R. § 1.17(t) are not required.

Applicant is still required to submit the reference in compliance with 37 C.F.R. § 1.78(a) by filling an amendment to the first sentence(s) of the specification or an ADS. See M.P.E.P. § 201.11.

Reasons for Allowance

The following is an Examiner's Statement of Reasons for Allowance: The claims are directed toward therapeutic suspensions for the treatment of HIV-1 infection comprising isolated and purified HIV-1 *nef*-deficient viral particles produced from cells transfected with a recombinant HIV-1 molecular clone comprising a *nef* deletion between the *Nco* I and *Xho* I sites. These compositions proved useful in the treatment of HIV infection (see the specification, Example 3, pages 19-24). Specifically, a double-blinded placebo controlled clinical study demonstrated that these compositions were effective at reducing the HIV-1 viral load. Administration of these compositions also resulted in increases in CD4⁺ T-cell counts and a positive clinical outcome (see specification, Tables II/III, pages 20-22). The closest available prior art was provided by Desrosiers (1998, U.S. Patent No. 5,851,813). Although this patent discloses the concept of making antigenic compositions comprising primate lentiviruses containing an engineered non-revertible mutation in the *nef* gene, nevertheless, it fails to suggest or teach that viral particles prepared from an HIV-1 *nef*-deficient molecular clone carrying the specifically claimed *Nco* I/*Xho* I mutation will display desirable properties (e.g., the ability to increase CD4⁺ T-cell levels; the ability to reduce the viral load; the ability to provide a positive clinical outcome; etc.). Moreover, the state-of-the-art at the time of filing vis-à-vis HIV-1 vaccine development was associated with a

considerable amount of unpredictability and failure. The role of Nef in HIV pathogenesis was still being ascertained and the general consensus argued against preparing and administering therapeutic compositions comprising HIV-1 *nef*-deficient viral particles (Johnson, 1999; Baba *et al.*, 1999; Hofmann-Lehmann *et al.*, 2003). It was not readily manifest to the skilled artisan if *nef*-defective viral particles would prove useful as a therapeutic, and in fact, the art suggested that such compositions might actually be detrimental. Accordingly, the claimed invention if free of the prior art and adequately supported by the disclosure.

Any comments considered necessary by applicant must be submitted no later than the payment of the Issue Fee and, to avoid processing delays, should preferably **accompany** the Issue Fee. Such submissions should be clearly labeled "Comments on Statement of Reasons for Allowance."

Correspondence

Any inquiry concerning this communication should be directed to Jeffrey S. Parkin, Ph.D., whose telephone number is (571) 272-0908. The examiner can normally be reached Monday through Thursday from 10:30 AM to 9:00 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Bruce R. Campell, Ph.D., can be reached at (571) 272-0974. Direct general status inquiries to the Technology Center 1600 receptionist at (571) 272-1600. Informal communications may be submitted to the Examiner's RightFAX account at (571) 273-0908.

Applicants are reminded that the United States Patent and Trademark Office (Office) requires most patent related correspondence to be: a) faxed to the Central FAX number (571-273-8300) (updated as of July 15, 2005), b) hand carried or delivered to the Customer Service Window (now located at the

Application No.: 10/811,725

Docket No. 14705

Applicant: Apte, S.

Filing Date: 03/29/2004

Randolph Building, 401 Dulany Street, Alexandria, VA 22314), c) mailed to the mailing address set forth in 37 C.F.R. § 1.1 (e.g., P.O. Box 1450, Alexandria, VA 22313-1450), or d) transmitted to the Office using the Office's Electronic Filing System. This notice replaces all prior Office notices specifying a specific fax number or hand carry address for certain patent related correspondence. For further information refer to the Updated Notice of Centralized Delivery and Facsimile Transmission Policy for Patent Related Correspondence, and Exceptions Thereto, 1292 Off. Gaz. Pat. Office 186 (March 29, 2005).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Respectfully,

/Jeffrey S. Parkin, Ph.D./
Primary Examiner, Art Unit 1648

31 August, 2008